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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte EVANGELYN C. ALOCILJA,
and ZARINI MUHAMMAD-TAHIR

Appeal 2009-1754
Application 10/074,499
Technology Center 1600

Decided:[1] February 23, 2009

Before DONALD E. ADAMS, ERIC GRIMES, and
LORA M. GREEN, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to an immunoassay device, which the Examiner has rejected as obvious. We have

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

This application was the subject of an earlier appeal to this board (Appeal 2006-2198, decided Sept. 18, 2006). In that appeal, we affirmed rejections of the then-pending claims for obviousness. The claims have since been amended and the rejections now on appeal have a different basis than the rejections previously affirmed. The earlier decision therefore has no bearing on whether the present claims are patentable over the evidence relied on by the Examiner in this appeal.

Claims 1-3, 7-10, 14-16, 18, 19, 21, 22, 24, and 26 are pending and on appeal. The claims subject to each rejection have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). Claims 1 and 22 are representative and read as follows:

1. A biosensor device which comprises:

a strip of a substrate having at least two zones wherein a

(1) first of the zones contains a first capture reagent bound to the substrate in a defined area between electrodes on different sides of the defined area for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second capture reagent directly bound to an electrically conductive polymer formed by oxidative polymerization of monomers and the polymer has been mixed to react with the second capture reagent to form a conjugate, wherein there is an absence of electrically conductive particles, wherein when a fluid sample containing an analyte is bound by the second capture reagent

to form a complex, the complex migrates to the first zone in the medium and the analyte is bound by the first capture reagent thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes to detect the analyte.

22. The device of Claim 1 or 2, wherein the biosensor device is a multi-array device comprising:

a plurality of first zones on the single strip of substrate, each of the first zones having a first capture reagent with a different specificity bound to the single strip of substrate between electrodes to immobilize one of multiple analytes on the single strip of substrate so that each of the multiple analytes can be detected simultaneously from the same sample on the single strip of substrate of the multi-array biosensor device.

The claims stand rejected under 35 U.S.C. § 103(a) as follows:

- Claims 1, 2, 7-9, 14-16, 18, 19, and 21 as obvious in view of Kim;[2]

and

- Claims 3, 10, 22, 24, and 26 as obvious in view of Kim and Roberts.[3]

OBVIOUSNESS BASED ON KIM

The Issue

The Examiner has rejected claims 1, 2, 7-9, 14-16, 18, 19, and 21 as obvious in view of Kim. The Examiner's position is that Kim's immunoassay device meets all the limitations of claim 1 except that it includes electrically conductive gold particles, and Kim suggests omitting

[2] Kim et al., "Conductimetric membrane strip immunosensor with polyaniline-bound gold colloids as signal generator," 14 Biosensors & Bioelectronics 907-915 (2000).
[3] Roberts et al., U.S. Patent 5,958,791, issued Sept. 28, 1999.

the gold particles, albeit in an unpreferred embodiment, thereby making obvious the device of claim 1 (Answer 4-5).

Appellants contend that Kim's disclosure would not have suggested omitting the gold particles from its immunocomplexes and in fact teaches away from doing so (see, e.g., Appeal Br. 11, 19).

The issue with respect to this rejection is: Did the Examiner err in concluding that Kim suggests omitting gold particles from its immunoassay device?

Findings of Fact

1. Kim discloses that, in a conventional sandwich immunoassay, "an aqueous medium containing analyte was absorbed by the capillary action from the bottom end of the strip system. . . . [T]he antigen-antibody reactions formed the sandwich complex containing gold particles, and a colored signal detectable by the naked eye was generated" (Kim 910, right-hand col.; Fig. 1).

2. Kim discloses that "[a]s an alternative method to colorimetry, the density of particulate gold, electron-rich metal, can be determined by measuring electric conduction" (*id.* at 911, left-hand col.).

3. Kim discloses an immunoassay (biosensor) device comprising a first zone that contains bound antibody in an area between two electrodes and a second zone that contains a second antibody conjugated to a gold particle (*id.* at Fig. 3).

4. Kim discloses that, when antibody/gold particle complexes were used in the disclosed system, "the electric conduction mediated by the gold colloids in the complex was proportional to the tracer concentration," but the

signal was weak and the maximum signal-to-noise ratio was half what could be achieved by photometry (*id.* at 911, right-hand col.).

5. Kim discloses that the poor performance of plain gold tracer

> could result from an impaired transfer of electrons along the gold particles. . . . The particles are surrounded with protein molecules, i.e. immunoglobulin and casein as blocking agent . . . that render an ionic polymer shell on the outside of the gold. This may interfere with electron hopping, a dominant process of charge-transfer between conducting mediators.

(*Id.* at 913, paragraph bridging the columns.)

6. Kim discloses that "[i]n an attempt to resolve the electronic barrier surrounding the gold, [they] introduced, on the surface, polymeric conductor molecules that may bridge the neighboring particles or at least bring them closer to improve the charge-transfer state" (*id.* at 913, right-hand col.).

7. Kim discloses that the conducting polymer used was a "water-soluble polyaniline . . . synthesized by oxidative polymerization of aniline monomer . . . incorporated onto the surface of gold particles . . . after immobilizing the antibody" (*id.* at 911, right-hand col.).

8. Kim discloses that polyaniline is an example of an organic polymer that "exhibit[s] metallic conductivity" and that "polyaniline is highly conductive upon protonation" (*id.* at 913, right-hand col.).

9. Kim discloses that the "protrusion degree of the polymer strands, acting as a wire (i.e. molecular wires) for electrical connection . . . mainly depends on the polymer concentration applied and the molecular dimension" (*id.*).

10. Kim concludes:

> An additional labeling agent comprising a conducting polymer to colloidal gold-antibody conjugates facilitated electric

> conduction between gold particles captured via antigen-antibody binding. *This strategy for conductimetric detection could be a better approach than direct labeling of the antibody with the polymer by chemical reaction* because, in such a case, the protein molecule itself does not contain available sites for electron relay.

(*Id.* at 914, right-hand col., emphasis added.)

Principles of Law

The test of obviousness is "whether the teachings of the prior art, taken as a whole, would have made obvious the claimed invention." *In re Gorman*, 933 F.2d 982, 986 (Fed. Cir. 1991).

"Obviousness is determined from the vantage point of a hypothetical person having ordinary skill in the art to which the patent pertains." *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998).

"Under 35 U.S.C. § 103, a reference must be considered not only for what it expressly teaches, but also for what it fairly suggests. . . . [W]e reiterate that 'all disclosures of the prior art, including unpreferred embodiments, must be considered' in determining obviousness." *In re Burckel*, 592 F.2d 1175, 1179 (CCPA 1979).

"The fact that the motivating benefit comes at the expense of another benefit. . . should not nullify its use as a basis to modify the disclosure of one reference with the teachings of another. Instead, the benefits, both lost and gained, should be weighed against one another." *Medichem S.A. v. Rolabo S.L.,* 437 F.3d 1157, 1165 (Fed. Cir. 2006).

Analysis

The Examiner has found, and Appellants do not dispute, that Kim discloses a device that meets all the limitations of claim 1 except for the requirement of "an absence of electrically conductive particles." The dispositive issue is whether the missing limitation is suggested by Kim's conclusion that a labeling agent comprising a conducting polymer together with a gold-antibody conjugate "could be a better approach than direct labeling of the antibody with the polymer by chemical reaction."

The Examiner interprets the above-quoted statement to mean "that such a direct labeling between the antibody and the conductive polymer was well known in the art at the time the invention was made" and concludes that it would have been obvious to directly label the antibody with polyaniline, in the absence of gold particles (Answer 5).

We agree with the Examiner's reasoning and conclusion. Kim discloses that polyaniline is a highly conductive polymer that overcomes the poor performance of plain gold particles as labels because it bridges the neighboring particles or brings them closer together. We agree with the Examiner that, when viewed in the context of its disclosure as a whole, Kim's statement that polyaniline/gold/antibody conjugates "could be a better approach the direct labeling of the antibody with the polymer" would have been understood to mean that direct labeling of the antibody with polyaniline would also have been expected to work in the disclosed assay, even if it had some disadvantages compared to labeling with gold plus polyaniline.

Appellants argue that "one skilled in the art reading Kim et al. would be directed away from eliminating the metal (gold) particles since Kim et al.

teaches that direct labeling of the antibody with the polymer would not have the electron relay sites on the antibody protein molecule which are necessary for conduction" (Appeal Br. 19).

We disagree. Appellants have pointed to nothing in Kim to show that electron relay sites on the antibodies are necessary for conduction. Although Kim's statement is somewhat ambiguous, we agree with the Examiner that it is most reasonably interpreted as saying that direct labeling of antibody with polyaniline would have been expected to work in the disclosed assay, even if it did not work as well in some respects as the polyaniline-plus-gold combination. That is, Kim's statement that polyaniline-plus-gold "could be a better approach" than polyaniline alone does not mean that polyaniline would not work, only that polyaniline-plus-gold might be expected to work better.

A prior art reference does not teach away from a particular approach just because it teaches that another approach has certain advantages; every alternative approach to a problem entails trade-offs. Kim reasonably suggests that direct labeling of antibody with polyaniline would work in its assay and therefore suggests the only limitation that distinguishes the device of claim 1 from the prior art device.

OBVIOUSNESS BASED ON KIM AND ROBERTS

The Issue

The Examiner has rejected claims 3, 10, 22, 24, and 26 as obvious in view of Kim and Roberts. The Examiner finds that Roberts teaches "a test device that includes multiple sets of interdigitated electrode arrays . . . in order to perform simultaneous multiple analyte detection" (Answer 7) and

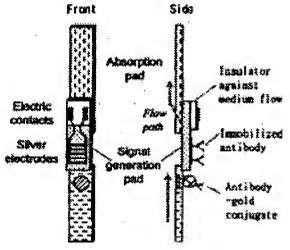
concludes that it would have been obvious to modify Kim's device to include the multiple sets of electrode arrays taught by Roberts, in order to allow detection of multiple analytes simultaneously (*id.*).

Appellants contend that Roberts would not have suggested the claimed device because the device taught by Roberts requires separate competitive binding portions and measurement portions to avoid cross-over signals (Appeal Br. 21-23).

The issue with respect to this rejection is: Did the Examiner err in concluding that Roberts would have suggested modifying Kim's device to comprise a plurality of electrode arrays to allow testing for multiple analytes simultaneously?

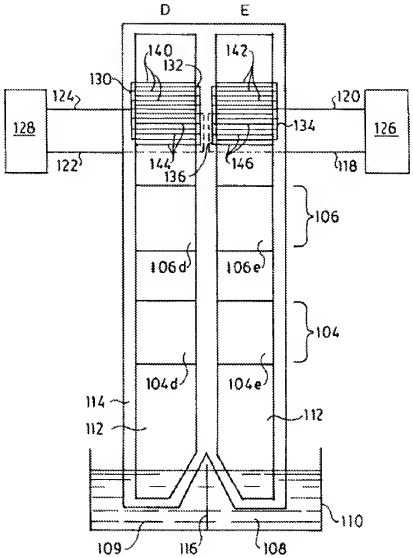
Additional Findings of Fact

11. Kim's Figure 3 is reproduced below:



The figure shows a schematic diagram of Kim's immunoassay device.

12. Roberts' Figure 1 is reproduced below:



The figure shows a schematic diagram of one embodiment of Roberts' device (Roberts, col. 8, ll. 41-43).

13. Roberts discloses that the device is "divided into two channels, namely, control channel D and test channel E" (*id.* at col. 15, ll. 6-7).

14. Roberts discloses that the device includes an electrochemical measurement portion that comprises fingers (140, 142) of a first conductor

(130, 134) interdigitated with fingers (144, 146) of a second conductor (132, 136).

15. Roberts discloses that the "electrochemical detection system . . . comprises an interdigitated set of microelectrodes and, optionally, a reference electrode" (*id.* at col. 23, ll. 28-30).

16. Roberts discloses that "the test device . . . may be modified for simultaneous multiple analyte detection or determination" (*id.* at col. 18, ll. 53-55).

17. Roberts discloses that "[w]ith the test devices and methods of the invention, one may also assay a test sample for a plurality of analytes . . . or screen for one or more of a plurality of analytes. In one embodiment, the test device includes multiple sets of interdigitated electrode arrays." (*Id.* at col. 25, ll. 16-20.)

Principles of Law

"[A]n implicit motivation to combine exists not only when a suggestion may be gleaned from the prior art as a whole, but when the 'improvement' is technology-independent and the combination of references results in a product or process that is more desirable, for example because it is stronger, cheaper, cleaner, faster, lighter, smaller, more durable, or more efficient." *Dystar Textilfarben Gmbh & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1368 (Fed. Cir. 2006).

Analysis

Claim 22 is directed to the device of claim 1, having a plurality of "first zones," at which are bound capture reagents with different

specificities. Kim would have made obvious the device of claim 1, for the reasons discussed above. Roberts discloses a similar device, also for electrochemical detection of analytes, that can comprise a plurality of electrochemical measurement portions with interdigititated microelectrodes. Roberts also discloses that the device can be modified to have multiple sets of interdigitated electrode arrays to screen for a plurality of analytes.

We agree with the Examiner that the combined teachings of Kim and Roberts would have made obvious the device of claim 22. Specifically, it would have been obvious to modify Kim's device to comprise a plurality of signal generation zones – containing an electrode array and different immobilized antibodies – in order to screen for a plurality of analytes simultaneously, because Roberts discloses a device for electrochemical detection of multiple analytes in a single assay and, as the Examiner noted (Answer 7), performing multiple tests at once is more efficient.

Appellants argue that "Roberts et al. does not teach a *single* multiple array as taught by Applicants as illustrated in Figure 3" (Appeal Br. 21). Appellants also argue that Roberts' device "would not suggest to a person of ordinary skill in the art the single multiple array as taught by Applicants, since the nature of the immunoassay and test device taught by Roberts et al. requires separate competitive binding portions 104 and measurement portions 106" (*id.* at 21-22).

This argument is not persuasive. The Examiner's rejection does not depend on modifying Kim's device to carry out the assay method disclosed by Roberts; the rejection is based on using Kim's assay to detect multiple analytes simultaneously by modifying Kim's device to have a plurality of

first zones comprising electrodes and capture reagents. (See Answer 13-14: "[T]he combination of Kim et al. in view of Roberts et al. . . . results in the device lay-out of Kim et al., wherein multiple electrode arrays (i.e. first zones) are included on the single substrate in order to perform simultaneous multiple analyte detection . . . as taught by Roberts et al.")

CONCLUSIONS OF LAW

The Examiner did not err in concluding that Kim suggests omitting gold particles from its immunoassay device, or that Roberts would have suggested modifying Kim's device to comprise a plurality of electrode arrays to allow testing for multiple analytes simultaneously.

SUMMARY

We affirm the rejection of claims 1, 2, 7-9, 14-16, 18, 19, and 21 under 35 U.S.C. § 103(a) based on Kim and the rejection of claims 3, 10, 22, 24, and 26 under 35 U.S.C. § 103(a) based on Kim and Roberts.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

dm

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